DOI:10.1111/j.1477-2574.2011.00390.x HPB

ORIGINAL ARTICLE

Pre- and intraoperative variables affecting early outcomes in elderly patients undergoing pancreaticoduodenectomy

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Abstract

Background: Conflicting data exist regarding the safety of pancreatic resections in elderly patients. In this study we compared early complication and mortality rates between patients younger and older than 80 years of age who underwent pancreaticoduodenectomy using a validated national database.

Methods: The National Surgical Quality Improvement Program (NSQIP) database for 2005–2009 was used for this retrospective analysis. The primary outcome measures for our analysis were 30-day postoperative mortality, major complication rate and overall complication rate.

Results: A total of 6293 patients who underwent PD for any cause were included in the analysis. Of these, 9.4% were aged ≥80 years. The incidence of 30-day mortality was significantly higher in patients aged ≥80 years (6.3%) than in those aged <80 years (2.7%). Older patients were also noted to have higher rates of overall complications and serious complications. On multivariate analysis, age, ASA (American Society of Anesthesiologists) classification, reduced functional status, history of dyspnoea, and need for intraoperative transfusion were risk factors associated with the occurrence of overall complications, serious complications and postoperative mortality.

Conclusions: This study shows that age among other factors is a determinant of postoperative morbidity and mortality following PD.

Keywords

pancreatic cancer, pancreaticoduodenectomy, elderly, functional status

Received 21 March 2011; accepted 2 August 2011

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Introduction

Pancreatic cancer is a disease that predominantly affects elderly people with a mean age at diagnosis of 72 years. Approximately 29% of patients with the disease are aged 75–84 years, and 13% are aged ≥85 years at the time of diagnosis.[1] According to the Surveillance, Epidemiology and End Results (SEER) Program, during 2003–2007 the median age at death from cancer of the pancreas in the USA was 73 years and approximately 30% of deaths occurred in patients aged 75–84 years, while 15% occurred in patients aged ≥85 years.[2] When therapy-associated mortality is taken into consideration, these rates increase even further. Despite recent new advances in chemotherapeutic regimens for advanced pancreatic cancers,[3,4] complete surgical resection continues to represent the only chance for cure. Pancreaticoduodenectomy (PD) is also performed in selected patients with chronic pancreatitis limited to the head of the gland.

Because of the increasing age of the general population, aggressive therapy is often offered to patients in the last years of their lives. However, previous studies have found conflicting results regarding morbidity and mortality associated with PD in elderly patients.[5,6] Proponents of surgical resection in the elderly population have found immediate postoperative complication rates similar to those in younger patients and comparable survival benefits.[7–9] Others have shown that elderly patients have a tendency to stay longer in the intensive care unit (ICU) following PD, have higher incidences of postoperative cardiac events, experience more nutritional and functional difficulties, and require more

readmissions compared with younger patients.[5,10] The purpose of the present study was to compare early complication and mortality rates between patients younger and older than 80 years of age who underwent PD for any cause. This research was accomplished using the database of the American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP), a nationally validated, outcomes-based project that quantifies 30-day risk-adjusted surgical outcomes at more than 200 hospitals across the USA.

Materials and methods

The NSQIP Participant User Files (NSQIP-PUF) for 2005–2009 were used for this retrospective analysis. Patients with a primary current procedural terminology (CPT) code for PD (CPT codes 48150, 48152, 48153 and 48154) were included for analysis. All PD procedures reported to the NSQIP were included in our study; analysis of the data was not limited to those procedures performed for oncologic reasons. The primary outcome measures were 30-day postoperative mortality, major complication rate and overall complication rate, as reported by other authors.[11] For analysis purposes, patients were considered to have sustained a major postoperative complication if they developed one or more of the following: organ/space surgical site infection; wound dehiscence; postoperative neurologic deficit (including stroke or coma for >24 h); cardiac arrest requiring cardiopulmonary resuscitation (CPR); myocardial infarction; bleeding requiring transfusion; pulmonary embolism; ventilator dependence for >48 h; progressive renal insufficiency; acute renal failure; and sepsis or septic shock. Patients were considered to have suffered any complication if they developed one or more of the following: a major complication (as defined above); superficial surgical site infection; deep surgical site infection; pneumonia; unplanned intubation; peripheral nerve injury; urinary tract infection; and deep venous thrombosis. Secondary outcome measures included the incidence of individual postoperative complications, need for reoperation, incidence and volume of intraoperative packed red blood cell (PRBC) transfusion, and postoperative length of hospital stay.

The primary predictor variable for our analysis was patient age, which was treated as a dichotomous variable (<80 years, ≥80 years). In the NSQIP-PUF, age is top-coded at 90 years. Other predictor variables included: female gender; body mass index >30 kg/m^2; American Society of Anesthesiologists (ASA) classification of ≥3; diabetes mellitus requiring therapy with non-insulin agents or insulin; smoking within 1 year of the operation; consumption of more than two drinks of ethanol per day in the 2 weeks prior to admission; dyspnoea upon moderate exertion or at rest; partially or totally dependent functional status prior to surgery (see definition below); chronic obstructive pulmonary disease (COPD); coronary artery disease (including history of myocardial infarction within the past 6 months, prior percutaneous coronary intervention, prior cardiac surgery and/or history of angina within 30 days prior to surgery); peripheral vascular disease (including history of revascularization or amputation for peripheral vascular disease and/or rest pain or gangrene); renal disease (including acute renal failure within 24 h prior to surgery and/or need for dialysis within 2 weeks prior to surgery); neurologic disease (including impaired sensorium, coma, hemiplegia/hemiparesis, history of transient ischaemic attacks, stroke with neurologic deficit, tumour involving the central nervous system, paraplegia/paraparesis and/or quadriplegia/quadraparesis); steroid use within 30 days prior to surgery for a chronic medical condition; chemotherapy for malignancy within 30 days prior to surgery; radiotherapy for malignancy within 90 days prior to surgery; need for intraoperative transfusion; and inclusion of pancreaticojejunostomy during PD (as indicated by CPT codes 48150 and 48153).

The NSQIP defines functional health status according to the patient's ability to perform activities of daily living (ADLs) during the 30 days prior to surgery. Activities of daily living include: bathing, feeding, toileting, and being mobile. The level of functional health status is defined by the following criteria and reported to the NSQIP as:

1 *Independent:* the patient does not require assistance from another person to fulfil any ADLs. This includes a person who is able to function independently using prosthetics, equipment or devices;
2 *Partially dependent:* the patient requires some assistance from another person to fulfil ADLs. This includes a person who utilizes prosthetics, equipment or devices but still requires some assistance from another person;
3 *Totally dependent:* the patient requires total assistance to fulfil all ADLs;
4 *Unknown:* patients whose functional status prior to surgery is not ascertained are reported as of unknown functional status. For analysis purposes, patients who were either partially or totally dependent were considered to have reduced functional status in this study.

Preoperative and intraoperative characteristics of patients aged <80 years and patients aged ≥80 years were compared using Pearson's chi-squared tests for categorical variables, unpaired two-sided Student's *t*-tests for normally distributed continuous variables, and Mann–Whitney rank sum tests for non-parametric continuous variables. For each primary outcome measure, a forward stepwise multivariate logistic regression model was developed using the previously described predictor variables. The *P*-value for entry of a variable into each model was < 0.05 and the primary predictor variable was forced into each model regardless of the significance of its association with the outcome measure on univariate analysis. Comparisons of secondary outcome measures in patients aged <80 years and patients aged ≥80 years, respectively, were performed using unpaired two-sided Student's *t*-tests for normally distributed continuous variables and Mann–Whitney rank sum tests for non-parametric continuous variables. STATA Version 11.0 (StataCorp LP, College Station, TX, USA) was used for all statistical analyses.

Table 1 Demographic and preoperative characteristics of patients undergoing pancreaticoduodenectomy (n = 6293) according to age

	Age: <80 years (n = 5700)	Age: ≥80 years (n = 593)	P-value[a]
Male gender, n (%)	2931 (48.7%)	332 (53.2%)	0.03
Body mass index > 30, n (%)	1455 (24.2%)	78 (12.5%)	<0.0001
ASA classification ≥ 3, n (%)	4089 (68.0%)	511 (82.0%)	<0.0001
Tobacco use, n (%)	1447 (24.1%)	33 (5.3%)	<0.0001
Ethanol use, n (%)	224 (3.7%)	10 (1.6%)	0.006
Reduced functional status, n (%)	159 (2.6%)	38 (6.1%)	<0.0001
Dyspnoea, n (%)	499 (8.3%)	83 (13.3%)	<0.0001
Coronary artery disease, n (%)	649 (10.8%)	112 (18.0%)	<0.0001
Hypertension, n (%)	3007 (50.0%)	455 (72.9%)	<0.0001
Renal insufficiency/failure, n (%)	25 (0.4%)	9 (1.4%)	0.001
Bleeding disorder, n (%)	141 (2.3%)	29 (4.7%)	0.001

[a]$P < 0.05$ was considered to indicate significance.
ASA, American Society of Anesthesiologists.

Table 2 Differences in postoperative complications and outcomes in patients undergoing pancreaticoduodenectomy according to age

	Age: < 80 years (n = 5700)	Age: ≥ 80 years (n = 593)	P-value[a]
Specific complication			
Wound dehiscence	102 (1.7%)	24 (3.9%)	<0.0001
Pneumonia	329 (5.5%)	49 (7.9%)	0.01
Unplanned intubation	295 (4.9%)	56 (9.0%)	<0.0001
Prolonged ventilator support	342 (5.7%)	60 (9.6%)	<0.0001
Urinary tract infection	331 (5.5%)	56 (9.0%)	<0.0001
Septic shock	286 (4.8%)	45 (7.2%)	0.007
Cardiac arrest requiring CPR	75 (1.3%)	14 (2.2%)	0.04
Myocardial infarction	26 (0.4%)	7 (1.1%)	0.02
Operative time, min, mean ± SD	377.5 ± 127.8	344.2 ± 109.4	<0.0001
Required intraoperative transfusion	1810 (30.1%)	250 (40.1%)	<0.0001
Postoperative length of stay, days, median	9 (range: 7–14)	11 (range: 8–18)	<0.0001

[a]$P < 0.05$ was considered to indicate significance.
CPR, cardiopulmonary resuscitation; SD, standard deviation.

Results

A total of 6293 patients who underwent PD were included in the final analysis. Of these, 593 patients (9.4%) were aged ≥80 years (median age: 82.9 ± 2.6 years). There were no differences in racial distributions between the groups and the majority of patients were White. There were no differences between groups in the number of patients with diabetes mellitus, COPD, peripheral vascular disease or neurologic disorder, the number of patients who received chemotherapy within 30 days or radiation therapy within 90 days prior to surgery, or the number of patients using steroids. Other demographic characteristics and preoperative variables for which statistically significant differences were found between groups are shown in Table 1.

The incidence of 30-day mortality was higher in patients aged ≥80 years (6.3%) than in those aged <80 years (2.7%) ($P < 0.05$). Older patients were also noted to have higher rates of overall complications (45.2% vs. 35.8%; $P < 0.05$) and serious complications (32.2% vs. 24%; $P < 0.05$). Elderly patients had significantly higher rates of wound dehiscence, pneumonia, unplanned intubation, prolonged respiratory support, urinary tract infections, septic shock, cardiac arrest requiring CPR and myocardial infarction (Table 2). These patients also required more intraoperative transfusions; however, the number of PRBC units transfused was similar in each group. Younger patients had a significantly shorter median postoperative hospital stay than their older counterparts (9 days vs. 11 days; $P < 0.05$). Complications which occurred at similar frequencies in both groups included stroke, coma for >24 h, peripheral nerve injury, deep venous thrombosis, sepsis, superficial surgical site infection, deep surgical site infection, organ/space surgical site infection, pulmonary embolism, progressive renal insufficiency and acute renal failure.

Table 3 Predictors of postoperative death after pancreaticoduodenectomy on multivariate analysis (using forward stepwise regression)

Predictor variable	Adjusted OR	95% CI	*P*-value[a]
Age ≥ 80 years	1.63	1.12–2.39	0.01
ASA classification ≥ 3	2.39	1.50–3.79	<0.0001
Reduced functional status	2.80	2.73–4.51	<0.0001
Dyspnoea	1.82	1.24–2.66	0.002
Coronary artery disease	1.46	1.02–2.10	0.04
Hypertension	1.50	1.08–2.08	0.015
Intraoperative transfusion	1.91	1.42–2.57	<0.0001

[a]$P < 0.05$ was considered to indicate significance.
OR, odds ratio; 95% CI, 95% confidence interval; ASA, American Society of Anesthesiologists.

The percentage of patients who required re-exploration was also similar in both groups.

On multivariate analysis, age was noted to be a significant risk factor for the occurrence of overall and serious complications, as well as for postoperative mortality (Tables 3–5). Other factors found to be predictors of complications and mortality included ASA class of ≥3, reduced functional status, history of dyspnoea, coronary artery disease, and history of intraoperative transfusions (Tables 3, 4). Risk factors that were predictors of any complication following PD are shown in Table 5. Female gender was found to be protective against both major [odds ratio (OR) 0.8, 95% confidence interval (CI) 0.71–0.90] and any (OR 0.89, 95% CI 0.80–0.99) complications after PD on multivariate analysis. The reasons for this are unclear.

Discussion

Contrary to previous studies that have reported age not to be an independent risk factor in patients undergoing PD,[12,13] our analysis of data sourced from a large national database shows that patients aged ≥80 years have a significantly higher risk for 30-day morbidity and mortality compared with younger patients. On multivariate analysis, age, ASA classification, reduced functional status, history of dyspnoea and need for intraoperative transfusion were found to be predictors of the occurrence of overall complications, serious complications and 30-day mortality. In concert with the findings of other authors,[14,15] our analysis shows that the need for intraoperative transfusions in patients undergoing PD is associated with poor postoperative outcomes. The higher incidence of intraoperative transfusions in the elderly group is not necessarily a sign of bleeding, poor surgical performance or tumour-related factors, but is more likely to be related to the higher incidence of baseline chronic diseases such as bleeding disorders and coronary artery disease in this population.

In elderly patients who present with pancreatic pathology such as pancreatic head masses, multiple factors should be considered before aggressive therapeutic protocols that include major surgical intervention are embarked upon. These patients typically use multiple medications that frequently must be continued during the postoperative period. Older patients tend to have a prior history of cardiac disease that requires close postoperative monitoring, and their nutritional status should be determined preoperatively because nutritional de-conditioning has been associated with poor postoperative outcomes after pancreatic resection.[16] Patients who are not completely dependent or whose ADL status, 'as defined' in this paper as decreased functional status, are at higher risk for the occurrence of postoperative complications and increased mortality. Indeed, multivariate analysis of our dataset showed that decreased functional status has the greatest predictive value for postoperative mortality after PD.

Although such factors are more common in elderly patients, most experts would not consider age alone to be a contraindication for PD based on the data available to date. In a recent retrospective study, Sohn *et al.* showed similar rates of longterm survival in younger and older patients undergoing PD for oncologic reasons.[17] However, in the present study, patients in the older group were found to have a longer postoperative length of stay and a higher rate of complications than younger patients. According to Sohn *et al.*, PD resulted in a perioperative mortality rate of 4.3% in the older group compared with 1.6% in the younger group, but the difference between these rates was not statistically significant.[17]

The use of a national validated database such as the ACS-NSQIP offers an incomparable opportunity to determine postoperative outcomes in a large number of patients treated at a variety of centres. Only recently, the NSQIP incorporated a procedure-targeted option that allows for the capture of hepatobiliary-specific outcomes in hundreds of patients.[18] A current limitation of the database and thus an inherent limitation of our study is the lack of information regarding frequent pancreas-related postoperative complications such as anastomotic leak, development of pancreatic fistula or delayed gastric emptying. Other limitations of the NSQIP and consequently of our study relate to the retrospective nature of the database. Most NSQIP data are collected by surgical clinical nurse reviewers, who abstract the medical record at the completion of the surgical portion of care.[19]

However, these restrictions have not prevented authors from using the database to establish risk calculators for patients undergoing pancreatic resection. A study by Parikh *et al.*, using the NSQIP database of patients who underwent all types of pancreatic resection, showed that risk factors for postoperative morbidity and mortality included age >74 years, male gender, BMI > 40 kg/m^2, preoperative sepsis, dependent functional status, ASA class >2, history of coronary heart disease, dyspnoea on moderate exertion, a bleeding disorder, and the contemplated procedure.[20] These findings are similar to ours in that advanced age, decreased functional status and need for intraoperative blood transfusion are associated with worse outcomes. However, Parikh *et al.*[20] included all pancreatic resections rather than focusing on PD only, as our study did. In addition, the study by Parikh *et al.*[20] was specifically

Table 4 Predictors of major complications after pancreaticoduodenectomy on multivariate analysis (using forward stepwise regression)

Predictor variable	Adjusted OR	95% CI	*P*-value[a]
Age ≥ 80 years	1.34	1.12–1.62	0.01
BMI ≥ 30	1.27	1.11–1.45	<0.0001
ASA classification ≥ 3	1.17	1.02–1.33	0.02
Reduced functional status	2.16	1.60–2.90	<0.0001
Dyspnoea	1.53	1.27–1.85	<0.0001
History of COPD	1.34	1.03–1.74	0.03
Coronary artery disease	1.23	1.03–1.46	0.02
Peripheral vascular disease	1.70	1.13–2.56	0.01
Bleeding disorder	1.66	1.20–2.30	0.002
Intraoperative transfusion	1.52	1.35–1.71	<0.0001

[a]$P < 0.05$ was considered to indicate significance.
OR, odds ratio; 95% CI, 95% confidence interval; BMI, body mass index; ASA, American Society of Anesthesiologists; COPD, chronic obstructive pulmonary disease.

Table 5 Predictors of any complication after pancreaticoduodenectomy on multivariate analysis (using forward stepwise regression)

Predictor variable	Adjusted OR	95% CI	*P*-value[a]
Age ≥ 80 years	1.35	1.14–1.60	0.001
BMI ≥ 30	1.28	1.14–1.45	<0.0001
Reduced functional status	1.94	1.43–2.61	<0.0001
Dyspnoea	1.49	1.25–1.78	<0.0001
Coronary artery disease	1.41	1.20–1.66	<0.0001
Bleeding disorder	1.95	1.42–2.68	<0.0001
Intraoperative transfusion	1.52	1.36–1.70	<0.0001

[a]$P < 0.05$ was considered to indicate significance.
OR, odds ratio; 95% CI, 95% confidence interval; BMI, body mass index.

designed to construct a risk calculator for pancreatic resections and not to compare outcomes between age groups.

Prior studies have shown that outcomes following pancreatic resections are related, at least partially, to the number of cases performed annually at a specific centre.[21] Although our analysis did not distinguish between low- and high-volume institutions, the management of elderly patients requires a full understanding of all aspects of health care that affect the geriatric population[22] and high-volume institutions often provide resources for these patients that lower-volume hospitals may not have available. The establishment of standards of quality for elderly patients should allow this population to be treated similarly to younger patients.[23] A recent analysis of SEER–Medicare linked data demonstrated that, in patients with locoregional pancreatic cancer, the likelihood of being evaluated by a surgeon decreased by 8% with each increasing year of age, and a decrease in surgical resection rates was noted regardless of patient comorbidities.[24] Even in patients without comorbidities, resection rates decreased from 40% in patients aged 66–70 years, to 37% in those aged 70–74 years, 32% in those aged 75–79 years, 21% in those aged 80–84 years, to only 7% in patients aged ≥85 years. Whether these findings demonstrate the reluctance of surgeons to offer PD to elderly patients or the preconceptions of primary doctors who refer these patients for surgical excision is not clear.

In conclusion, the analysis of a nationally validated database shows increased morbidity and mortality rates in elderly patients undergoing PD for any cause. In this study, reduced functional status was found to have the greatest predictive value for postoperative mortality after PD. Other factors affecting outcomes include ASA classification, history of dyspnoea and need for intraoperative transfusions. The referral of elderly patients to centres which have dedicated geriatric services is advisable when possible. Age and functional status should be taken into consideration when counselling patients on the morbidity and mortality associated with this operation.

Conflicts of interest

We have no conflict of interest.

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